REMARKS

Claims 16-18 are pending and being examined.

The only remaining rejection is under 35 U.S.C. §112, first paragraph. Applicants request reconsideration of the outstanding rejections.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

In paragraphs 1–5 of the Office Action, the Office rejects claims 16 and 17, under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to use the invention. In particular, the Office contends that the specification fails to provide an adequate description of "other cell lines" which can be used for the invention.

Applicants respectfully disagree.

35 U.S.C. §112 requires that, "the specification contain a written description of **the invention**, and ... enable any person skilled in the art to which it pertains, to make and use the **same** ..." (emphasis added). One is not required to enable any more than what is claimed. The Patent Office is improperly imposing a requirement that Applicants demonstrate "commercial success" to meet the enablement requirement of 35 U.S.C. §112.

The specification as originally filed discloses actual enabling experiments embodying the claimed methods. Further, Applicants have disclosed the requisite starting materials and the use thereof needed to practice the full scope of the invention.

For example, at page 15, line 23, Applicants disclose what kind of cells can be used as starting materials for the present invention. In detail, the specification discloses that "any cell can be utilized, since the resulting location of fluorescence can be visualized as either in the cytoplasm or in the nucleus". Further the specification describes that "additionally, for such detection events, cells having increased copy number of the binding site, in an array, can be used". Therefore, the present specification clearly teaches that any mammalian cell having a plurality of steroid response elements in an array such that the element can be directly detected can be used to perform the screening for a ligand that activates the translocation of the steroid receptor to the nucleus. By a plurality of steroid response elements is meant that the number of copies of the elements is greater than one (page 17, line 18). It has been known for higher eukaryotic genomes to contain naturally occuring repetitive sequences (page 65, line 11). Therefore, any mammalian cell which meets these criteria can by used as a starting material for the present invention. Additionally, the specification describes the localizations of the elements to be "in sufficiently close physical proximity along a chromosome, either present endogenously or artificially introduced or induced, or in extrachromosomally replicating episomes" (page 17, line 11; page 19, line 10). Methods for artificially introducing or inducing a gene into chromosomes are well known in the art (e.g., see specification at page 18, lines 28-30 and page 19, lines 1-2), as are transformation or transfection methods for extrachromosomally replicating episomes. Nevertheless, examples for these methods are given in the specification of the invention (e.g. page 42, line 11; page 61, line 18). A non-limiting example of an artificially modified cell including a high number of copies of the response elements is the cell line 3134 which is described in the application in detail and which is deposited with American Type Culture Collection as accession number CRL-11998 (ATTC) (e.g. page 17, line 27). This cell line is particularly useful for detection of ligands. The same results can be achieved by the use of any desired (naturally occurring or artificially modified) mammal cell having a plurality of steroid response elements in such an array; as stated above.

Further, the Office asserts that the specification fails to provide an adequate description as to how the alternative cells are to be used for the invention.

The Applicants believe that the specification discloses all aspects of the claimed invention.

The requirements of 35 U.S.C. §112, first paragraph, are fulfilled where one skilled in the art could use the invention, given the specification disclosure, without undue experimentation[3]. Undue breadth is analyzed in terms of whether it would have involved undue experimentation to achieve the claimed invention. The determination of what constitutes undue experimentation in a given case, requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art[4].

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed[5].

In *Ex parte Forman*, the Board set forth the following criteria for undue experimentation:

> The question of undue breadth is analyzed in the view of:
>
> (1) the quantity of experimentation necessary,
>
> (2) the amount of direction or guidance presented,
>
> (3) the presence or absence of working examples,
>
> (4) the nature of the invention,
>
> (5) the state of the prior art,

---

[3] *In Re Eynde,* 480 F2d 1364, 178 USPQ 470 (CCPA 1970).
[4] *Ex parte Forman, et al.*, 230 USPQ 546, 547 (BPAI 1986).
[5] *Ex parte Forman, et al.*, 230 USPQ 546, 547 (BPAI 1986).

(6) the relative skill of those in that art, and

(7) the unpredictability of the art[6].

The unpredictability of the art is only one factor that must be evaluated and weighed with the other factors.

The specification provides adequate written description of examples of steroid response elements in an array where the steroid nuclear receptor is ER, AR, GR, PR, and MR (page 13, line 20; page 17, line 8; page 18, line 4; page 50, line 25; and page 51, line 1). With regard to ER, Applicants teach the sequence of the steroid response element in the specification at page 59, line 4 and methods for making it in the specification at page 59, line 5 and line 14. With regard to GR, Applicants teach the sequence of the steroid response element at page 59, line 3 and line 10. With regard to AR, PR, and MR, the consensus sequence of each of these steroid response elements are the same, and each receptor can bind to the steroid hormone-responsive elements that are recognized by GR.

The Applicants have demonstrated translocation of the steroid receptor to the nucleus of a mammalian cell (page 47, lines 1; page 48, line 1) as part of a screening assay to find ligands that activate the translocation of a steroid receptor to the nucleus in a mammalian cell. In one embodiment, the ligand is dexamethasone and a dose response curve for dexamethasone is provided (page 47, line 1). In another embodiment, the ligand is RU486 (page 47, line 27; page 48, line 1). In yet another embodiment, the ligand is progesterone (page 48, line 5). When a non-ligand for a particular receptor is used to treat a fluorescent receptor, no translocation is observed, demonstrating importance of activating the steroid receptor for translocation to occur from cytoplasm to the nucleus (page 48, line 7).

---

[6] *Forman* at page 547, supra.

Further, the claims fully enable the use of any mammalian nucleated cell in the claimed methods because the steroid hormone signal transduction pathway is conserved in all eukaryotic cells, including mammalian cells, and translocation or movement of a steroid receptor from the cytoplasm to the cell nucleus is a necessary step for steroid receptors to modulate steroid hormone-responsive gene expression by steroid hormones.

As evidenced by the above, Applicants have provided ample post filing confirmatory data that shows the successful use of Applicants methods, namely how to screen for a ligand that activates the translocation of a steroid receptor to the nucleus in a mammalian cell.

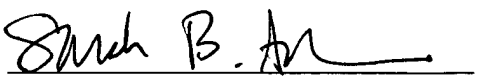
Hence, no undue experimentation would be required to practice the claimed invention. Accordingly, Applicants respectfully request that the Office withdraw the rejection.

CONCLUSION

Applicants believe that all grounds for rejection of the claims have been successfully overcome and that the claims are now in condition for allowance. Withdrawal of the Examiner's remaining rejections is requested and prompt allowance of the claims is solicited. If any issues remain in connection with the claims, the Examiner is encouraged to contact the undersigned by telephone to discuss the same.

No fee, other than the $225.00 for two-month extension fee, is deemed necessary in connection with the filing of this Communication. If any further fee is necessary, the Patent Office is authorized to charge any additional fee to Deposit Account No. 50-0306.

Respectfully submitted,



SaraLynn Mandel
Registration No. 31,853
Sarah B. Adriano
Registration No. 34,470
Mandel & Adriano
55 South Lake Ave., Suite 710
Pasadena, California 91101
(626) 395-7801
Customer No: 26,941